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Short Communications

Hypoglycaemic activity of arecoline in betel nut *Areca catechu* L.*

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Subcutaneous administration of the alkaloid fraction of *A. catechu* in doses ranging from 0.05 to 0.50 mg/kg body weight and subsequent monitoring of blood sugar levels showed that dosages at 0.20 and 0.25 mg/kg body weight were responsive. The hypoglycaemia lasted for 4-6 hr. Bioassay studies showed a simulated action with the synthetic product.

Betelnut (*Areca catechu* L.) has been assigned several medicinal and pharmacological properties in ancient ayurvedic texts and in British and German Pharmacopoiea. These properties are mainly due to the alkaloids present therein. Among the alkaloids, arecoline constitutes the major fraction and is considered to be more reactive. The present study aims at determining the effect of arecoline on blood sugar levels in artificially induced diabetes which can further throw light on the feasibility of this alkaloid as a drug.

Induction of alloxan diabetes—The experiment was carried out on male albino rabbits weighing 1.4 kg on an average. Diabetes was induced in the rabbits by a single iv injection of alloxan monohydrate in distilled water at the rate of 140 mg/kg body weight. The animals were fasted 36 hr before injection. Insulin (Protamine-Zinc, Boots) was given sc at the rate of 0.8 units/100 g body weight for 5 days after alloxan injection. This was to reduce the mortality due to alloxan toxicity. Rabbits showing pronounced hyperglycaemia after 7 days (blood sugar levels above 230 mg/100 ml) were selected for the experiment. The final grouping of the animals was as follows:

Four animals were used in each group. Group I, Control (normal rabbits), Group II, Diabetic, Group IIIa-e, Diabetic rabbits given sc injection of arecoline at the rate of 0.05, 0.1, 0.2, 0.25 and 0.5 mg/kg body wt respectively.

Preparation and administration of test material—Arecoline was extracted from finely ground arecanut powder as follows:

The powder was defatted using chloroform, for 10-14 hr in a soxhlet extraction set and successively extracted with alcohol. The alcoholic extract was subjected to partition chromatography at varying *p*H by employing chloroform and 2 *N* H_2SO_4, to separate the arecoline and non-arecoline fraction[1]. The amount of arecoline present in the extract was estimated colorimetrically by following the method of Bishenbaev *et al.*[2]. The purity of the arecoline fraction was tested by two-dimensional TLC using Silica gel G.

The extract was administered sc to fasting rabbits in Group IIIa-e in the above mentioned dosages. The

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Table 1—Effect of arecoline on blood sugar levels of diabetic rabbits

Group (III)	Dosages of arecoline (mg/kg body wt)	Blood sugar values (mg/100 ml blood)								
		0 hr	1 hr	2 hr	3 hr	4 hr	5 hr	6 hr	7 hr	8 hr
a	0.05	232	225	219	228	220	218 (6.03%)	232	231	243
b	0.10	242	230	215 (10.11%)	219	223	229	231	235	248
c	0.20	238	201	180	180	156	121	114 (52.1%)	175	216
d	0.25	239	191	166	151	143	120 (49.7%)	120 (49.7%)	169	210
e	0.50	234	228	215 (8.11%)	217	222	216	226	220	223

Mean of 4 values from 4 rabbits per group. SE/plot, 13.50; Gen. mean, 204.60; CV (%), 6.60; CD (%), 6.78.
Values in parentheses denote the maximum percentage effect (decrease).

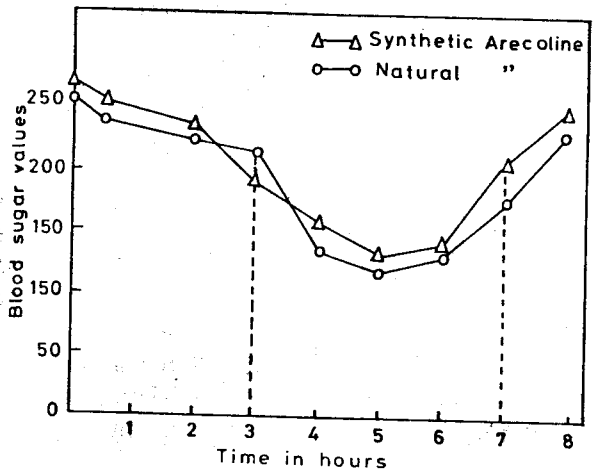

Fig. 1—Bioassay studies on extracted arecoline. A simulative response with the synthetic product is seen on blood sugar levels.

effect of the natural product was compared with that of the synthetic sample.

Monitoring of sugar levels—Blood sugar levels were determined prior to the administration of the alkaloid. Blood was taken from the marginal ear vein of the rabbits by a single needle prick. The sugar levels were estimated by the method of Asatoor and King modified by Nelson[3]. Monitoring was continued at 1 hr intervals up to a period of 8 hr or until the levels reversed to the original value.

Table shows the blood sugar levels at 1 hr intervals along with the original values. It is seen that dosages at 0.05, 0.1 and 0.5 mg/kg body weight (groups a, b and e) do not exert any effect on sugar levels, while dosages of 0.2 and 0.25 mg/kg body weight (groups c & d) cause a reduction lasting for 4 hr. 6 hr after adminstration, the sugar levels show a gradual increase and tend to reach the original values. A reduction of 52.1% and 49.7% respectively is seen at dosages of 0.20 and 0.25 mg/kg body weight.

Figure 1 shows the results of the bioassay of the extracted alkaloid. It is clear that the natural product at the rate of 0.20 mg/kg body weight stimulates the effect of the same dose of synthetic arecoline in reducing the sugar levels.

Thus, administration of the alkaloids at the two specific doses (0.20 and 0.25 mg/kg body weight) causes hypoglycaemia in the diabetic state. The comparative efficacy of arecoline in this aspect as seen for a short period (4-6 hr) was tested using other oral hypoglycaemic agents like tolbutamide (orinase) and phenformin (DBI-TD). With these two drugs, the effect lasts for 10-12 hr, but only at higher doses. In case of arecoline, the effect, though short, is brought about with very small doses of the material. However, it should be pointed out that the above data show the response of arecoline to diabetes and it warrants a further study on its toxic effects. This study is an attempt to find out the duration of hypoglycaemia exhibited by arecoline and its optimum dose for maximum response.

References

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